Amendments to the Drawings:

The replacement drawings submitted on May 12, 2006 were objected to for inclusion of new matter. The Applicants thank the Examiner for recognizing the inadvertent shift in the alignment of some of the sequences. Applicants have submitted herewith replacement Figures 1 and 2 in which the alignment has been corrected in Figure 1 to reflect the alignment provided in the originally filed drawings. Accordingly, Applicants respectfully request withdrawal of the objection to the drawings.

The Examiner further states that the description of Figure 1 on pages 3-4 of the specification discusses amino acids that are highlighted in black and gray, and that such highlighting is not present in the drawing. However, the specification was amended in the response filed May 12, 2006 to remove reference to the shading in Figure 1.

REMARKS

Status of the claims

Claims 1-11, 19, 22, and 23 are pending in the present application. Amendments of a formal nature have been made to claims 1 and 19. No new matter has been added by way of this amendment.

Amendments to the Specification

The specification has been amended to correct a typographical error in the description of example conserved residues in SEQ ID NO:3. Correction of this error does not introduce new matter as the corrected residues in SEQ ID NO:3 are clearly depicted as conserved in the originally filed drawings (i.e., black shading with reversed text).

The Objection to the Claims Should Be Withdrawn

The Examiner has objected to the claims because of informalities in claims 1 and 19. Claim 1 has been amended to recite "and" at the end of part (c). Claim 19 has been amended to insert --the method-- before "comprising." Therefore, the objection to the claims should be withdrawn.

The Rejections Under 35 U.S.C. § 112, First Paragraph, Should be Withdrawn

Enablement

The Examiner rejected claims 1-11, 19 and 22-23 under 35 U.S.C. § 112, first paragraph, on the grounds that the specification does not enable one skilled in the art to make or use the invention. This rejection is respectfully traversed.

The Examiner asserts that the specification, while enabling for nucleic acids encoding SEQ ID NO:3 or 5, host cells, plants, plant cells and seeds comprising them, and a method of using them to make SEQ ID NO:3 or 5, does not reasonably provide enablement for methods and compositions drawn to nucleic acids encoding pesticidal proteins with 90% sequence identity to SEQ ID NO:3 or 5, nucleic acids with 90% identity to SEQ ID NO:1, 2, or 4, or host cells,

plants, plant cells and seeds comprising them, and a method of using them to make a pesticidal protein with 90% identity to SEQ ID NO:1, 2 or 4. The Examiner states that the specification fails to provide guidance for which amino acids of SEQ ID NO:3 or 5 can be altered and to which other amino acids, and which amino acids must not be changed, to maintain the activity of the encoded protein, as well as which regions of the protein can tolerate insertions and still produce a functional protein.

The Examiner appears to be suggesting that, in order to satisfy the enablement requirement, Applicants must provide support for making an amino acid with up to 219 substitutions that could be used to successfully practice the invention, such that no experimentation would be required. According to the applicable case law, however, the test of enablement is not whether experimentation is necessary to make and use an invention, but rather if experimentation is necessary, whether it is undue. *In re Angstadt*, 198 USPQ 214, 219 (C.C.P.A. 1976). Furthermore, a considerable amount of experimentation is permissible if it is merely routine or if the specification provides a reasonable amount of guidance in which the experimentation should proceed. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988).

The test of whether an invention requires undue experimentation is not based on a single factor, but rather is a conclusion reached by weighing many factors. *Id.* at 1404. Factors to be considered in determining whether undue experimentation is required include the quantity of experimentation necessary, the amount of guidance provided in the specification, the presence of working examples of the invention in the application, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability in the art, and the breadth of the claimed invention. *Id.* Accordingly, the holding of *Wands* does not require that Applicants provide as working examples every pesticidal polypeptide that could be used to practice the present invention, or a pesticidal polypeptide with 219 amino acid substitutions as the Examiner asserts. Rather, *Wands* sets out factors to be considered in determining whether undue experimentation is required to make and use the invention.

The Examiner maintains that the specification does not enable one of skill in the art to make and use nucleic acids that encode polypeptides that retain pesticidal activity and have at least 90% sequence identity to SEQ ID NO:1, 2, or 4, or 90% sequence identity to a nucleotide

sequence that encodes SEQ ID NO:3 or 5. The Examiner incorrectly bases this conclusion solely on the number of possible nucleic acids having the recited percent identity to SEQ ID NO:1, 2 or 4, or a nucleotide sequence encoding SEQ ID NO:3 or 5 while continuing to dismiss the other factors set forth in *Wands* for assessing whether undue experimentation is required.

First, sufficient guidance for making and using the recited sequences is present in the specification. The claimed variants and fragments of SEQ ID NO:1, 2, or 4, or nucleotide sequences encoding SEQ ID NO:3 or 5 are limited by a percent identity (i.e., 90% identity) and further limited by the functional requirement that they possess pesticidal activity. Guidance for preparing variants and fragments of SEQ ID NO:1, 2, or 4, or nucleotide sequences encoding SEQ ID NO:3 or 5 and for determining percent identity is provided in the specification and generally known in the art. See page 8, lines 22-27, and pages 9-13. Numerous delta-endotoxins were also well known in the art at the time the application was filed. See Crickmore *et al.* (1998) *Microbiol. Molec. Biol. Rev.* 62:807-813, which is incorporated by reference on page 2, lines 8-9 and was submitted with the response filed on May 12, 2006. The necessary molecular biology and mutagenesis techniques for preparing the variants and fragments of pesticidal sequences of the invention are routine. Moreover, methods for assessing the pesticidal activity of a polypeptide are readily available in the art and provided in the specification. See, for example, page 11, lines 22-26 and Examples 7, 10, 11 and 12.

In order to identify the pesticidal sequences encompassed by the present claims, one of skill in the art would only need to prepare variants and fragments of the nucleotide sequence of SEQ ID NO:1, 2, or 4, or a nucleotide sequence encoding SEQ ID NO:3 or 5, having the specified characteristics recited in the claims (e.g., at least 90% identity) and then assay these polypeptides for pesticidal activity. Routine methods for preparing variants and fragments and testing the resulting polypeptides for pesticidal activity are known in the art and described in the specification. Although some experimentation is required to practice the claimed invention, it is now customary in the art to generate a large number of sequences and to test them in a large-scale assay for a desired function, and, therefore, such experimentation is not undue, particularly in view of the routine nature of the required methods. Contrary to the Examiner's conclusions, in order to identify variants and fragments of the nucleotide sequence of SEQ ID NO:1, 2, or 4,

or a nucleotide sequence encoding SEQ ID NO:3 or 5 that could be used in the invention, a person skilled in the art would only need to utilize standard molecular biology and mutagenesis techniques and routine screening tests for pesticidal activity. Therefore, given the level of skill and knowledge in the art, the availability of standard methods and assays, and the significant guidance provided in the specification, Applicants respectfully submit that the amount of experimentation required to identify delta-endotoxins and variants and fragments thereof having pesticidal activity and the structural features recited in the claims is routine, not undue.

In support of the argument that the invention is not enabled throughout the full scope of the claims, the Examiner continues to rely on *Genentech, Inc. v. Novo Nordisk, A/S*, 42 USPQ 2d 1001, 1005 (Fed. Cir. 1997) which, according to the Examiner, teaches that disclosure of a "mere germ of an idea does not constitute [an] enabling disclosure", and that "the specification, not the knowledge of one skilled in the art" must supply the enabling aspects of the invention.

As discussed in the response filed November 15, 2006, the question before the Court in *Genentech* was whether the specification of U.S. Patent 5,424,199 would have enabled a skilled artisan to use cleavable fusion expression to make hGH without undue experimentation. The Court concluded that the specification does not describe in any detail whatsoever how to make hGH using cleavable fusion expression, and that no description of any specific cleavable conjugate protein appears. Contrarily, in the instant specification, specific nucleotide sequences encoding proteins with pesticidal activity, as well as fragments thereof, are provided (SEQ ID NO:1, 2, and 4), and sufficient guidance for preparing variants and fragments of SEQ ID NO:1, 2, or 4, or nucleotide sequences encoding SEQ ID NO:3 or 5, and for determining percent identity is provided in the specification.

Further, although the Court does state that the "mere germ of an idea does not constitute an enabling disclosure", it immediately follows with the opinion that "[w]hile every aspect of a generic claim certainly need not have been carried out by an inventor, or exemplified in the specification, reasonable detail must be provided in order to enable members of the public to understand and carry out the invention." In citing *Hybritech Inc. v. Monoclonal Antibodies, Inc.* 802 F.2d 1367, 1385, 231 USPQ 81, 94 (Fed. Cir. 1986), the Court reiterates that "a specification need not disclose what is well known in the art" and characterizes "undue experimentation" as

that in which "there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out".

The Examiner asserts that the specification fails to provide the reasonable detail for making the nucleic acids within the full scope of the claims. However, the instant specification clearly provides starting material (SEQ ID NO:1-5) as well as extensive description regarding the conditions under which amino acid substitutions can be carried out to generate a nucleotide sequence with at least 90% sequence identity to SEQ ID NO:1, 2, or 4, or a nucleotide sequence that encodes an amino acid sequence that is at least 90% identical to SEQ ID NO:3 or 5. For instance, the specification describes examples of conserved residues that are not likely to tolerate substitution (see page 13), delineates conserved domains characteristic of delta-endotoxin proteins (see page 4), and highlights conserved residues in the sequences of the invention (see Figure 1 as originally filed). Further, routine methods for preparing variants and fragments and testing the resulting polypeptides for pesticidal activity are described in the specification.

The Examiner also relies on *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at 1027 in support of rejection of the claims for lack of enablement. Similar to the *Genentech* decision, the opinion provided by the Court in *Amgen* further supports the enablement of the present invention. As noted by the Examiner, the Court acknowledges that the disclosure in the Amgen patent (which provides a few EPO analog genes) "might well justify a generic claim encompassing these [EPO analog genes] and similar analogs". The Court ruled that the disclosure was inadequate support for Amgen's desire to claim *all* EPO gene analogs. There is no such claim in the instant application. Rather, the claims encompass specific nucleotide sequences (SEQ ID NO:1, 2, and 4), as well as nucleotide sequences with at least 90% sequence identity to SEQ ID NO:1, 2, or 4, or nucleotide sequences that encode an amino acid sequence that is at least 90% identical to SEQ ID NO:3 or 5 (i.e., "similar analogs"). Therefore, the Applicants contend that the claims at issue in the *Amgen* decision are not related to the claims of the instant application, and that the opinion expressed by the Court in this decision actually *supports* the Applicants assertion that the claims are fully enabled.

The Examiner disagrees with the Applicants position on the Amgen decision and states that no similar analogs of SEQ ID NO:3 or 5 were provided in the instant specification (page 11

of the February 6, 2007 Office Action). However, the Court acknowledges that the disclosure of the few EPO genes justifies a claim encompassing those genes *and similar analogs*. Likewise, the disclosure of SEQ ID NO:3 and 5, with guidance on which amino acids are likely to tolerate substitutions, justifies a claim to SEQ ID NO:3 and 5, as well as claims to similar analogs (e.g, 90% identity).

The Examiner also asserts that the position of the Applicant is that conservative substitutions are fine and nonconservative ones verboten (page 16 of the February 6, 2007 Office Action). While the instant specification does not exclude the possibility that functional variants may have minor conserved or nonconserved alterations in conserved residues, it does teach that, "[i]n general, such substitutions would not be made for conserved amino acid residues, or for amino acid residues residing within a conserved motif..." (page 13, lines 10-12 of the instant specification). Therefore, as noted in the response filed on November 15, 2006, the Applicants do not presume that every conceivable conservative substitution in a nonconserved region will produce a protein with the recited activity, rather that the methods for making and testing substitutions within 90% sequence identity to SEQ ID NO:3 or 5 is routine in the art, and the level of experimentation is not undue.

The Examiner continues to rely on the teachings of Guo *et al.* (2004) *Proc. Natl. Acad. Sci. USA* 101:9205-9210 for the proposition that making amino acid substitutions in SEQ ID NO:3 or 5 would need to be done randomly, that random substitutions have a likelihood of failure, and that the likelihood of failure amounts to undue experimentation. The Examiner notes that Guo *et al.* did not find any isolates with more than 11 amino acid substitutions in a 298 amino acid long protein, and that this data suggests that 219 amino acid substitutions cannot be made in SEQ ID NO:3. However, this data only suggests that a large number of substitutions *were* not produced by Guo *et al.*, not that they *could* not be produced. Furthermore, as discussed extensively herein, the specification provides sufficient guidance with respect to which amino acids are not likely to tolerate substitutions such that the making of amino acids with at least 90% sequence identity to SEQ ID NO:3 or 5 *does not* require "random" substitution.

Further, detailed information about the structure of delta-endotoxins was also known in the art. See, for example, Li *et al.* (1991) *Nature* 353:815-821 (describing the crystal structure of

the Cry3A protein), which is incorporated by reference on page 12 of the specification, and Morse *et al.* (2001) *Structure* 9:409-417, both of which were submitted with the May 12, 2006 response. Delta-endotoxins are extremely well-characterized and related to each other to various degrees by similarities in their amino acid sequences and tertiary structures. A combined consideration of the published structural analyses of delta-endotoxins and the reported functions associated with particular structures, motifs, and the like indicates that specific regions of the toxin are correlated with particular functions and discrete steps of the mode of action of the protein. The Examiner dismisses the teachings of Li and Morse because they do not provide guidance for making 219 amino acid substitutions in a 629 amino acid long protein. However, Li *et al.* and Morse *et al.* do provide guidance for determining the regions of a delta-endotoxin that would tolerate modification, which can be used to rationally design a 629 amino acid long protein with up to 219 amino acid substitutions. Such guidance eliminates the need to make random substitutions.

For example, based on the regions of delta-endotoxins that are conserved among protein family members, the skilled artisan could choose among possible modifications to produce polypeptides within the structural parameters set forth in the claims and then test these modified variants to determine if they retain pesticidal activity. In light of the guidance provided in the specification and the state of the art with respect to delta-endotoxins, a skilled artisan could readily conclude which amino acids are essential for structure and function and could envisage similar sequences that are 90% identical to the nucleotide sequence of SEQ ID NO:1, 2, or 4, or a nucleotide sequence encoding SEQ ID NO:3 or 5, and that retain pesticidal activity. As such, one of skill in the art could identify the pesticidal sequences encompassed by the present claims without undue experimentation.

The Examiner cites de Maagd *et al.* (2001) *Trends in Genetics* 17:193-199, Aronson *et al.* (2001) *FEMS Microbiology Letters* 195:1-8, de Maagd *et al.* (1999) *Appl. Environ. Microbiol.* 65:4369-4374, Tounsi *et al.* (2003) *J Appl. Microbiol.* 95:23-28, Angsuthanansombat *et al.* (2001) *J. Biochem. Mol. Biol.* 34:402-407 in support of the argument that making substitutions in Cry proteins is unpredictable and that toxicity must be determined empirically. However, each of these references supports the position of the Applicants that making

substitutions and testing for activity is routine in the art.

The Examiner further maintains that the specification does not enable the transformation of any plant with a nucleotide sequence with 90% identity to the nucleotide sequence of SEQ ID NO:1, 2, or 4, or a nucleotide sequence encoding SEQ ID NO:3 or 5 because undue trial and error experimentation would be required to screen for nucleotide sequences encompassed by the claims and plants transformed therewith to identify those plants with pesticidal activity. As discussed above, the amount of experimentation required to identify a nucleotide sequence that has 90% sequence identity to SEQ ID NO:1, 2, or 4, or to a nucleotide sequence encoding SEQ ID NO:3 or 5 is not undue. Given the guidance provided in the specification and the knowledge in the art, the claims directed to transformation of a plant with a delta-endotoxin sequence, or variant or fragment thereof, are fully enabled.

In light of the above arguments, the level of skill and knowledge in the art, and the guidance provided in the specification, Applicants respectfully submit that the specification is enabling for the full scope of claims 1-11, 19, 22 and 23. Thus, the rejection of the claims under 35 U.S.C. § 112, first paragraph, for lack of enablement should be withdrawn.

Written Description

Claims 1-11, 19, 22 and 23 were further rejected under 35 U.S.C. § 112, first paragraph, as failing to satisfy the written description requirement. The rejection is respectfully traversed.

The Examiner asserts that the disclosure is insufficient to support claims that are drawn to a genus of nucleic acids having 90% sequence identity to SEQ ID NO:1, 2, or 4, or nucleic acids encoding polypeptides having 90% identity to SEQ ID NO:3 or 5.

In order to satisfy the written description requirement of 35 U.S.C. § 112, the application must reasonably convey to one skilled in the art that the applicant was in possession of the claimed subject matter at the time the application was filed. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d (BNA) 1111, 1117 (Fed. Cir. 1991). Every species encompassed by the claimed invention, however, need not be disclosed in the specification to satisfy the written description requirement of 35 U.S.C. § 112, first paragraph. *Utter v. Hiraga*, 845 F.2d 993, 6 USPQ2d 1709 (Fed. Cir. 1988). The Federal Circuit has made it clear that

sufficient written description requires simply the knowledge and level of skill in the art to permit one of skill to immediately envision the product claimed from the disclosure. *Purdue Pharm L.P. v. Faulding In.*, 230 F.3d 1320 1323, 596 USPQ2d 1481, 1483 (Fed. Cir. 2000) ("One skilled in the art must immediately discern the limitations at issue in the claims.").

Moreover, the "Guidelines for Examination of Patent Applications Under 35 U.S.C. §112, ¶ 1, 'Written Description' Requirement" state that a genus may be described by "sufficient description of a representative number of species . . . or by disclosure of relevant, identifying characteristics , *i.e.* structure or other physical and/or chemical properties." *Id.* at 1106. This is in accordance with the standard for written description set forth in *Regents of the University of California v. Eli Lilly & Co*, 119 F.3d 1559 (Fed. Cir. 1997), where the court held that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, or chemical name' of the claimed subject matter sufficient to distinguish it from other materials." 119 F.3d at 1568, citing *Fiers v. Revel* 984 F.2d 1164 (Fed. Cir. 1993). In *Enzo Biochem, Inc. v. Gen-Probe, Inc.*, 323 F.2d 926 (Fed. Cir. 2002), the Federal Circuit adopted the PTO standard for written description, stating:

> [U]nder the Guidelines, the written description requirement would be met . . . if the functional characteristics of [a genus of polypeptides] were coupled with a disclosed correlation between that function and a structure that is sufficiently known or disclosed. We are persuaded by the Guidelines on this point and adopt the PTO's applicable standard for determining compliance with the written description requirement."

The claims of the present application meet the requirements for written description set forth by the Federal Circuit. The claims as amended recite that the nucleic acid have 90% sequence identity to the nucleotide sequence of SEQ ID NO:1, 2, or 4, or to a nucleotide sequence encoding SEQ ID NO:3 or 5. Methods for determining percent identity between any two sequences are known in the art and are provided in the specification. See pages 8-13. As discussed above, nucleotide sequences for full-length AXMI-004 (SEQ ID NO:1), as well as variants and fragments (e.g., SEQ ID NO:2 and 4) are disclosed in the specification. Numerous delta-endotoxin sequences were also generally known in the art at the time the application was

filed. Moreover, detailed information regarding the structure of delta-endotoxins and the reported functions associated with particular structures, regions, and motifs was also available in the prior art as well as discussed in detail on page 2, lines 22-29, Figure legend 1, and on pages 12-13.

At the time of filing, it was known that delta-endotoxins generally comprise three domains, a seven-helix bundle that is involved in pore formation, a three-sheet domain that has been implicated in receptor recognition, and a beta-sandwich motif. See Li *et al.* (1991) *Nature* 305:815-821. Thus, the recitation of polypeptides having a particular percent identity to a delta-endotoxin provides very specific and defined structural parameters of the sequences that can be used in the invention. These structural limitations are sufficient to distinguish the nucleotide and amino acid sequences of the invention from other nucleic acids and polypeptides and thus sufficiently define the genus of sequences useful in the practice of the present invention.

The Examiner maintains that the specification describes no relevant characteristics or motifs for the claimed nucleic acids other than identity to SEQ ID NO:1, 2, or 4, and that the level of skill and knowledge in the art at the time of filing is such that no other proteins within the scope of the claims were known. Applicants acknowledge that no other proteins within the scope of the claims were known; hence, the novelty of the invention. However, Applicants respectfully disagree with the assertion that no relevant characteristics or motifs were disclosed. As discussed above, domains associated with specific functions were known (Li *et al.*, *supra*), and conserved regions within each of these functional domains are described in the specification. Although the Examiner dismisses the relevance of these teachings since they describe a cry3Aa protein (page 14 of the February 6, 2007 Office Action), Li *et al.* state that the overall structure of this delta-endotoxin represents the general fold of the family of active delta-endotoxin proteins (see the abstract of Li *et al.*), and that the core of the cry3Aa molecule is built from the five sequence blocks that are highly conserved throughout the delta-endotoxin family (column 2, page 817 of Li *et al.*). These highly conserved sequence domains have been described in the instant specification as they relate to the delta-endotoxin of the invention.

The Examiner is also reminded that the description of a representative number of species does not require the description to be of such specificity that it would provide individual support

for each species that the genus embraces. 66 Fed. Reg. 1099, 1106 (2000). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. 66 Fed. Reg. 1099, 1106 (2000). Here, Applicants have provided nucleotide and amino acid sequences for exemplary pesticidal sequences and variants and fragments thereof encompassed by the claims. Moreover, numerous delta-endotoxin sequences were known and readily available in the art. Therefore, Applicants submit that in view of the present disclosure and the knowledge and level of skill in the art the skilled artisan would envision the claimed invention.

The description of a claimed genus can be by structure, formula, chemical name, or physical properties. *See Ex parte Maizel*, 27 USPQ2d 1662, 1669 (B.P.A.I. 1992), *citing Amgen v. Chugai*, 927 F.2d 1200, 1206 (Fed. Cir. 1991). A genus of polypeptides may therefore be described by means of a recitation of a representative number of amino acid sequences that fall within the scope of the genus, *or* by means of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. *See Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1569 (Fed. Cir. 1997); *see also* Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, first paragraph, "Written Description" Requirement, 66 Fed. Reg. 1099, 1106 (2000). The recitation of a predictable structure (i.e., an amino acid sequence having a specified percent identity or number of contiguous amino acid residues of a particular sequence) is sufficient to satisfy the written description requirement. Thus, the application provides the structural features that characterize sequences having at least 90% sequence identity to SEQ ID NO:1, 2, or 4, or to a nucleotide sequence encoding SEQ ID NO:3 or 5 that retain pesticidal activity.

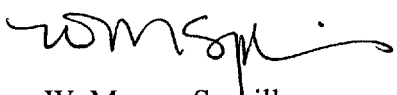
An Applicant may also rely upon functional characteristics in the description, provided there is a correlation between the function and structure of the sequences recited in the claims. *Id.*, citing *Lilly* at 1568. The present claims further recite functional characteristics that distinguish the sequences of the claimed genus. Specifically, the claims as amended recite that the sequences having at least 90% sequence identity to SEQ ID NO:1, 2, or 4, or to a nucleotide sequence encoding SEQ ID NO:3 or 5 encode proteins which have pesticidal activity. The

specification and the art provide standard assays that may be used to measure pesticidal activity. See, for example, page 8, lines 27-31. Furthermore, as noted above, Applicants have disclosed fragment sequences that retain pesticidal activity (e.g., SEQ ID NO:4, which encodes a fragment of SEQ ID NO:3). Accordingly, both the structural and functional properties that characterize the genus of sequences that can be used to practice the invention are specifically recited in the claims. The sequences that fall within the scope of the claims can readily be identified by the methods set forth in the specification.

In summary, the specification provides an adequate written description of the claimed invention. In particular, the specification provides: nucleotide and amino acid sequences for pesticidal toxins, and variants and fragments thereof, that fall within the scope of the claims; guidance regarding sequence alterations that do not disrupt pesticidal activity of a toxin; guidance for determining percent identity; and methods for assaying the pesticidal activity of proteins. In view of the above remarks and claim amendments, Applicants submit that the relevant identifying structural and functional properties of the genus of sequences of the present invention would be clearly recognized by one of skill in the art. Consequently, Applicants were in possession of the invention at the time the application was filed, and the rejection of the claims under 35 U.S.C. § 112, first paragraph, for lack of written description should be withdrawn.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



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CUSTOMER NO. 00826 **ALSTON & BIRD LLP** Bank of America Plaza 101 South Tryon Street, Suite 4000 Charlotte, NC 28280-4000 Tel Raleigh Office (919) 862-2200 Fax Raleigh Office (919) 862-2260	**ELECTRONICALLY FILED USING THE EFS-WEB ELECTRONIC FILING SYSTEM OF THE UNITED STATES PATENT & TRADEMARK OFFICE ON MAY 4, 2007.**